

Public Health Research in Chronic Disease

By JOHN E. DUNN, Jr., M.D.

THE changing nature of the health problems that burden our society is becoming increasingly apparent. The severe outbreaks and epidemics of the infectious and communicable diseases are giving way to the endemicity of chronic disease.

"Chronic disease" as a generic term usually conjures up such entities and groups of diseases as heart disease, cancer, mental diseases, and diabetes. Actually, the connotation is broader than the mere disease label. There is the added implication of insidious progression, slow and incomplete recovery, disability, necessity for adaptation on the part of the affected individual, and the host of services—medical, nursing, social, economic, housekeeping, rehabilitation—involved in the struggle between an individual and a chronic disease from which he is trying to recover or with which he is learning to live. A definition adopted by the Conference on the Preventive Aspects of Chronic Disease in 1951 (1) states that "chronic disease comprises all impairments or deviations from nor-

mal which have one or more of the following characteristics: (a) are permanent; (b) leave residual disability; (c) are caused by nonreversible pathological alteration; (d) require special training of the patient for rehabilitation; and (e) may be expected to require a long period of supervision, observation, or care." Although one might wish to quibble with some of the details of this definition, it paints the picture of chronic disease essentially as seen through the eyes of the victim. The summation of such victims in a community delineates the problem of public health.

A definition of chronic disease has been considered; it would seem unnecessary to define research. Here too, however, there are differences of opinion as to what should be included in the term. Such modifying adjectives as "applied," "field," "clinical," "epidemiological," and "administrative" are used to distinguish the fuzzy limits of what can be encompassed by so jealously guarded a term as research. If we consider research as a quest for knowledge and view the chronic disease problem from the vantage point of public health responsibility, we are immediately impressed with the fragmentary nature of knowledge and the rather general ignorance of the whole spectrum of chronic diseases and their chronology from etiology to recovery, symbiotic stabilization, or death. In this discussion research in chronic disease is considered in its broadest sense and from the standpoint of public health responsibility. Since I am working in the can-

Dr. Dunn is a field investigator with the Field Investigations and Demonstrations Branch of the National Cancer Institute, National Institutes of Health, Public Health Service, assigned to the bureau of chronic diseases, California State Department of Public Health. This paper was presented at the 1955 meeting of the Western Branch of the American Public Health Association, Phoenix, Ariz.

cer field, I will draw on that subject for illustrative purposes.

Areas of Research

Chronic diseases and conditions are problems of public health for one or more of the following reasons: (a) their relative importance as causes of death; (b) their responsibility for prolonged disability, during which time the affected individual is not self-sufficient, with all that this implies; and (c) the ability of the community, through organized effort, to meet many of the problems that are difficult or insoluble for the individual.

Public health has a need of knowledge of the whole chronology of chronic disease, from the characteristics, habits, and surroundings of individuals that give them a special proclivity for a certain disease or diseases, as, for example, current interest in obesity and cigarette smoking, to the requirements of the individual with stabilized disease which will return him to an active, useful life. The chronology of chronic disease for the purpose of this discussion can be conveniently, although somewhat arbitrarily, divided into the following stages: (a) the pre-disease period, during which the unknown and suspected etiological factors are operating; (b) the incipient stage, when the disease is recognizable by some clinical or laboratory means but is not yet symptomatic; (c) the full-blown symptomatic stage; (d) stabilization of the disease process and maximal recovery; and (e) restoration of the patient to useful life. The first two stages are the most appealing to preventive medicine and public health and the actual or potential means for attacking chronic diseases at these stages have been designated primary and secondary prevention, respectively (1). The third stage, of course, is the period for skilled medical management. The fourth and fifth stages are periods when the individual is in greatest need of assistance and services from various community resources, that may or may not exist, in his effort to become an active useful person again.

Etiology

It is difficult to deal with a disease empirically. It is understandable, then, why primary

interest should center on laboratory and clinical research to elucidate the etiological and pathogenic mechanisms of the chronic diseases. We have only to look at the tremendous increase in the amount of money that has been made available for medical research in recent years, much of which is directed toward study of the etiology and pathogenics of the chronic diseases, to realize the urgency felt for knowledge to combat the ever-increasing burden of disability and death for which these diseases are responsible. It is estimated that in 1952 the Nation spent an estimated \$180 million for medical research; 42 percent came from government sources; 33 percent, from industry; 14 percent, from private philanthropy; and 11 percent, from hospitals and medical schools. The total amount is a tenfold increase over the expenditures for medical research of a decade before (2). In 1952, the Public Health Service administered \$18 million of grant funds to support medical research in addition to the funds for its own growing research program. The recent opening of the Clinical Center of the National Institutes of Health is a big step forward in furthering the research effort toward solving the problem of chronic disease development.

Almost every scientific discipline of the biological and natural sciences is represented somewhere on the research team attacking the array of morbid processes included in the chronic diseases; and research interest ranges from a study of the simplest biological systems to the response of whole organisms to experimental conditions. The volume of research findings is tremendous and is not easily synthesized into a total picture. However, there can be little doubt that the picture can be completed and the etiology and pathogenesis of the chronic diseases understood. From the public health vantage point, these research developments are to be viewed with keen interest and hope that better means of anticipating, diagnosing, and treating the chronic diseases will evolve.

Despite the momentum that chronic disease research is gathering, there is still the feeling that insufficient emphasis is being directed toward certain approaches to the study of the occurrence of chronic disease (3, 4). This stems partly from a lack of personnel with disciplinary training oriented to the chronic

disease problem and partly from the lack of research equipment and techniques having the precision and accuracy of those available to the laboratory investigator. I am referring to the epidemiological study of chronic diseases. Man is a complex animal who has evolved a complex and largely artificial social structure within which to live. Not all economic and technological progress is necessarily good for him in a biological sense. He eats too much, smokes too much, drinks too much, and lives under too much tension. Evidence is accumulating to indicate that these, and other factors much less obvious, play a part in the occurrence of chronic disease. Epidemiologically speaking, then, the soil should not be neglected in preoccupation with the seed. Epidemiology is primarily a tool of public health.

Cancer has perhaps received more attention, meager and superficial as it has been, than any of the other chronic diseases regarding the characteristics and attributes of people that are related to the occurrence of the disease. Most of this comes under the classification of descriptive epidemiology and has perhaps served to raise more questions than it has answered. Much of what has been learned in cancer epidemiology, or endemiology as some would prefer to call it, has had to come from existing data, such as mortality records, or from short-term retrospective studies that could be handled with limited finances. Nevertheless, some rather clear-cut and specific findings have come out of such investigations, such as bladder cancer as a result of beta-naphthylamine exposure in the aniline dye industry, chromate cancer in the chromate industry, the direct relationship of the amount of solar radiation and the frequency of skin cancer, the relative immunity of Jewish women to cervical cancer, and, more recently, the association of cigarette smoking and lung cancer. Other established associations are in need of further explanation. Cancer of certain sites has been shown to exhibit a socioeconomic gradient. For example, cancer of the upper gastrointestinal tract and stomach and cancer of the cervix show an increasing incidence as economic status decreases. A gradient in the opposite direction is shown by cancer of the breast and ovary. These findings originated from studies carried on in England and,

later, in Denmark. Recently, studies to determine the existence of such gradients in this country have been undertaken, one of which is nearing completion for San Francisco. The findings of these several studies differ in certain details but confirm the fact that cancer of certain sites does have socioeconomic gradients.

Isolated studies concerning cancer of the cervix have shown association of this disease with a multiplicity of variables, including the fact of marriage, age at marriage, childbearing, economic status, stability of marriage, syphilis, circumcision of spouse, and race. Certainly, there is need and opportunity for unraveling this multiplicity of variables, many of which are correlated with each other.

Recently, there has been a trend toward use of the more expensive and time-consuming, but much more satisfactory, prospective type of epidemiological approach. Perhaps this indicates a more general realization of the contribution that the methods of epidemiological study can make to the problems of the chronic diseases. The findings relative to cigarette smoking and lung cancer have been confirmed by such studies in both this country and England (5, 6). A byproduct of considerable importance from both of these studies was the finding that cigarette smoking is also associated with coronary heart disease. A finding such as this could not, of course, come from a retrospective study of lung cancer patients. A study is now under way in California in which the lung cancer risk of certain occupations is being determined. A previous study of the case-control type indicated that certain occupations carried an increased risk of lung cancer. At the present time, populations of workers engaged in these suspect occupations are being assembled, and their lung cancer experience will be determined over the next several years by checking all cancer deaths among males occurring in the State against these assembled populations.

It was determined that populations of 5,000 to 10,000 individuals would be necessary in order to have a reasonable expectancy of lung cancer mortality during the study period. Data on such large numbers would be difficult to collect from industrial establishments, and mailed

questionnaires became of necessity the method for collecting data. Union organizations seemed to offer the best means of gaining access to the occupational groups to be studied. The union organizations have proved to be very cooperative and the percentage of mailed questionnaires completed and returned has ranged between 85 and 90 percent, a most gratifying response. It is expected that the more than 25,000 workers that have entered the study will be increased three- or fourfold before the study populations are closed.

A few years ago a long-term study of heart disease was undertaken in Framingham, Mass., in which some 5,000 individuals were examined. These individuals will be followed over the next several years to determine the factors associated with the occurrence of heart disease. A study of coronary heart disease among London double-deck bus operators showed that conductors had fewer and milder cases of the disease than did drivers (7). It was hypothesized that the greater physical activity demanded of conductors in their work might be responsible for this finding. This explanation was supported by similar differences found for physically active and sedentary workers among postal workers and civil servants.

From these illustrations, it should be clear that the epidemiological method can make significant and worthwhile contributions to the understanding of the occurrence of chronic disease. Perhaps the time has come for public health workers to take a more active part in contributing what can be learned from population studies to these problems that are destined to absorb most of our interest and efforts in the near future.

Incipient Stage and Case Finding

It is generally agreed that diseases are more effectively treated if they are recognized in their early stages. This is particularly true for the chronic diseases where progressive and more or less permanent damage is a prominent feature of the pathological processes. In cancer control, the whole program is based on the concept of early recognition and treatment since success or failure is clearly centered on the time when metastasis occurs.

The problems connected with recognition of

the incipient stage of chronic disease are two-fold: What techniques do we have for their recognition? How do we use them effectively? These two questions are intimately related to each other. A procedure that is technically difficult, time consuming, and expensive is hardly adaptable to examining the general population for unsuspected disease, for example, conventional gastrointestinal series for X-ray examination of the alimentary canal for possible cancer. On the other hand, procedures that are technically suitable for general application but lack sensitivity, specificity, or both will fail from lack of efficiency. An example would be a cancer test based on quantitative changes in the normal serum proteins that occur with this disease, or these diseases, as some prefer.

Dissatisfaction with the number of cases of symptomatic tuberculosis that were coming to diagnosis in the advanced stages led to technological development of miniature X-ray films and successful mass application of the new technique to screening the general population for cases of minimal, asymptomatic tuberculosis. Similar applications have been made of syphilis serology. Cancer detection centers were an outgrowth of this concept. It was natural to extend the concept to multiphasic screening, that is, combining screening procedures to look for a number of diseases simultaneously. So far, attempts to apply this method of identifying incipient and asymptomatic diseases have been sporadic and isolated. Reactions to these attempts have varied. They have been condemned as poor medicine and bad public health (8). However, multiple screening is considered to have a place if it can be meshed with the normal flow of patients through medical channels, such as physicians' offices, outpatient departments, hospitals, and industrial medical examinations (9).

The basic question, however, seems to me to be whether screening procedures can be the means for bringing the diseases in question under medical management in an incipient or asymptomatic stage rather than in the symptomatic stage when diagnosis is usually made. This implies two things: (a) making the procedures available to the general population, or to those segments at major risk from the diseases being sought, as a direct service and not

as a tie-in or bonus feature of some other medical service; and (b) screening the population at risk periodically, the frequency to be determined from knowledge of the usual period between the time the screening procedure can first indicate presence of the disease and the time the disease will become manifest.

One important question is, How frequently should a screening procedure be repeated? Initial multiphasic screening of a population largely deals with prevalence of undiagnosed disease. Prevalence is the product of incidence times duration. If one disease has one-fifth the incidence of a second disease in a given population, but the former existed 5 years on the average asymptotically and the latter, 1 year, the findings in terms of numbers of cases of the two diseases in an initial screening will be the same. However, annual repetition of the screening would produce only one-fifth the number of new cases of the first disease, whereas the second disease would continue to be found in the same numbers. Perhaps repetitive screening for the first disease could effectively and economically be done on a 3- to 5-year cycle. The second disease is committed to annual screening.

One means of evaluating the accomplishments of multiphasic screening would be to compare the course of the cases of a disease so identified with the course of the same disease when first recognized symptomatically. Here we may be misled. Many diseases show a range of rates of progression. The slower-developing and more benign forms of the disease accumulate disproportionately among the undiagnosed, asymptomatic, cases of prevalent disease. Under these circumstances the prognosis for the prevalent cases as a group is more favorable than the prognosis for the incident cases.

Cancer is a disease for which more is at stake in earlier diagnosis perhaps than in any other of the so-called chronic diseases. Among the diseases usually grouped in the chronic disease category, symptomatic cancer is one of the more acute. It is primarily a killer, having the dubious distinction of ranking second in this capacity. Cancer is not found among the chronic diseases listed as responsible for the greatest amount of disability, either in terms of individual cases or collectively for all cases of specific diseases.

Since clinically recognizable cancer, that is, gross tumors that are obvious to direct or X-ray visualization, is such an acute disease, we have a narrow margin of time within which to accomplish asymptomatic diagnosis as a substitute for symptomatic diagnosis. Furthermore, we are forced to search for individual tumor masses at all the sites where they frequently occur because there is no established general pathophysiological change yet discovered associated with the development of cancer that is qualitatively or quantitatively sufficiently unique to serve as a general test procedure.

The cure rate for lung cancer, which has increased so remarkably in recent decades, is negligible when the disease has become symptomatic. Lung tumor masses can be identified in chest X-ray films before symptoms occur. Is this an effective and practical screening procedure for cancer of the lung? The lung cancer results of the Los Angeles mass X-ray survey suggest that X-ray screening can identify cases somewhere in the range of 9 months to a year prior to symptomatic diagnosis. Is this enough earlier to influence prognosis? There is some evidence from the Los Angeles data that it is (10), although the improvement still leaves much to be desired. Is the amount of improvement in prognosis real or are the results biased by an undue proportion of slower-growing tumors that can be expected among prevalent cases, as commented on earlier? Other sources of bias are likely in a survey of this type, and the results therefore cannot be regarded as definite. If it is felt that periodic X-ray chest examinations at 6-month intervals has real promise as a means of bettering the prognosis of lung cancer, it is worth a thorough, properly designed study of repetitive examinations in the same population.

The best example of a more hopeful aspect of discovering asymptomatic cancer is the use of exfoliative cytology for cancer of the cervix uteri. Contrary to what was said earlier regarding clinically recognizable cancer (visible gross lesions), the study of cervical cancer with cytology, whereby microscopic lesions without gross abnormality can be identified, suggests that cancer may be a very chronic disease, with the clinical stage as usually recognized being the explosive and lethal phase. The evidence

indicates that there is a preinvasive stage that lasts for several years. Periodic searching for evidence of this lesion, which would seem to be almost certainly curable, may be successfully accomplished at 2-, 3-, or 4-year intervals. A study now in progress in Memphis, Tenn. (11), is using exfoliative cytology to determine whether cervical cancer can be made a relatively nonlethal disease when the general population of females is periodically screened by this procedure. Unfortunately, the cytological method is not well adapted to screening for other sites of cancer because of the technical difficulties of obtaining specimens.

The more important questions relative to the substitution of asymptomatic diagnosis for symptomatic diagnosis of the chronic diseases are:

1. What procedures do we have that are technically suitable for mass application?

2. How efficient are these procedures in terms of sensitivity and specificity when used in the asymptomatic general population?

3. What is the pattern of the specific diseases that are being sought in terms of incidence, prevalence, age, and sex selection, and so on?

4. How much earlier, on the average, can the screening procedure pick up the specific disease than it is usually diagnosed as a result of symptoms?

5. As a corollary to this, what is the cyclic frequency for most practical and efficient use of the screening procedure?

6. What is the advantage in prognosis for cases of the disease identified by the screening procedure as compared to those progressing to symptomatic diagnosis?

If intelligent and efficient use is to be made of the concept of multiple screening, such questions as these must be answered no matter how the method is to be applied. If the idea is to be effective in improving the total chronic disease picture, it must be promoted in some organized plan in making it continuously available for any population group. Public health has traditionally taken the leadership in case-finding methods and has most to gain from answering questions such as those proposed. This knowledge is needed if we expect to do more than enumerate for demonstration purposes the number of unattended and undiagnosed dis-

eases and defects that are prevalent in any population in which symptoms are the usual basis for seeking medical attention.

Symptomatic Clinical Disease

The symptomatic clinical stage is the stage of disease for skilled medical management. And the emphasis here is on treatment. The therapeutic advances made and being made are spectacular and become matters of public knowledge almost as rapidly as they appear. The antibiotics have become so well established and are available in such variety to meet almost every special purpose for combating infectious agents, that we accept them as part of our medical heritage. The sulfa drugs, which were the marvel of their day, have already passed into that heritage. Current developments in the manipulation of hormones to influence the course of certain chronic diseases, using the concept of metabolic antagonists in cancer chemotherapy, more effective antihypertensive drugs, and so on, are examples of important progress in therapy for the chronic diseases.

Much of the fundamental research that is being so extensively carried on is directed to an understanding of the basic chemical processes of metabolism in the normal state, in disease, and under the influence of therapeutic agents. Interest includes the cellular components identified with metabolic functions; hormonal effects on cellular metabolism and tissue function; the in vivo fate of therapeutic agents in terms of chemical alteration of the agent, specific action in chemical and functional terms, storage, and excretion; and the chemical nature and physical-chemical state of nutritional elements during blood transport, in tissue fluids, and body storage. The development and perfection of research tools such as radioactive isotopes, electron and phase microscopy, electrophoresis, paper chromatography, and high-speed centrifugation have done much to make this detailed and exacting research possible. Many of the advances in specific means of controlling infection, in understanding of the physiological economy of the body, and in improved anesthesia have made possible the extension of surgical procedures in the cardiovascular, cancer, and other fields.

Out of this extensive medical and biological

research is certain to come an understanding of the detailed mechanism of many of the chronic diseases and, from this understanding, the development of many specific and potent therapeutic agents will follow.

This is a phase of chronic disease research which is not directly related to public health responsibility. Interest has been extended to an evaluation of the efficacy of therapy, such as the use of tumor registries in the cancer field. Therapeutic advances can have considerable effect on the community load of the disabled and incapacitated chronically ill which is a direct interest and responsibility of public health.

The Chronically Ill Population

The philosophy of chronic disease control is to prevent and to mitigate the burden of chronic disease that is now prematurely disabling and incapacitating large numbers of our population. It has been estimated that 4,000,000 persons in the United States are continually victimized by these conditions, three-fourths of them under 65 years of age (12). Even with postponement of death through control of disease there will always be a need for community services for those reaching the incapacity of old age and terminal illness (13).

Public Health Responsibility

How can public health assay its responsibilities for the chronic diseases without defining the problem in terms of numerical size; relative importance of the various diseases and injuries in terms of incidence and prevalence; nature of the incapacities; type of care being given, by whom, and in what degree of adequacy; unmet needs and who can best provide them; availability of community services and facilities; possibilities for rehabilitation and the availability of this service; and a host of other questions that require answering as the chronic disease problem is dissected and analyzed? A number of morbidity studies are going on now—in New Jersey, Baltimore, and the State of California—to answer many of these questions. In other studies, such as that of the Community Studies, Inc., of Kansas City, Mo., the possibilities and cost of rehabilitating the handicapped and chronically ill are being determined.

The generalizations that can be drawn from these studies will be helpful in gaining insight and in providing guidelines for understanding and planning programs to aid and rehabilitate the chronically ill. Each community, however, will have to examine its own problem, do the best it can with what it has, and attempt to discover and rectify its weaknesses. Such community introspection perhaps cannot be graced with the designation of research, but here is where the problem and the solution lie for the care and rehabilitation of our chronically ill.

Summary and Conclusions

1. The chronology of chronic disease is considered from the standpoint of public health interest and responsibility.
2. There has been greatly increased financial support for research directed toward the chronic diseases in recent years, with major emphasis on laboratory and clinical research.
3. The epidemiological method, primarily a tool of public health, has been relatively neglected as a research approach to studying the chronic diseases.
4. Case-finding methods have been inadequately evaluated. A number of questions are posed that must be answered before these methods can be used intelligently and with predictable results.
5. Laboratory and clinical research will eventually elucidate the mechanisms of many of the chronic diseases. Some of these findings will be found adaptable for practical application as preventive measures. These findings should also be scrutinized for adaptation as more discriminatory case finding methods.
6. Advances in therapeutic management give promise of better control of the chronic diseases from the standpoint of stopping or delaying progression before disability and incapacity result.
7. As of now, however, there is a sizable and growing burden of chronic illness and disability among our people which will always be with us in some degree. Public health has the responsibility of studying the problem and contributing its skills to the prevention and control of these diseases, and the support and rehabilitation of those affected.

REFERENCES

- (1) Proceedings of the Conference on the Preventive Aspects of Chronic Disease. Sponsored by the Commission on Chronic Illness. Raleigh, N. C., Health Publications Institute, Inc., 1951, p. 14.
- (2) U. S. President's Commission on the Health Needs of the Nation: Building America's Health, Volume 1, Findings and Recommendations. Washington, D. C., U. S. Government Printing Office, 1952, p. 39.
- (3) Notes and Comments. A contemporary opinion about cancer. *The Medical Officer* 93: 56, Feb. 4, 1955.
- (4) Morris, J. N.: Use of epidemiology. *Brit. Med. J.* No. 4936: 395-401, Aug. 13, 1955.
- (5) Hammond, E. C., and Horn, I.: The relationship between human smoking habits and death rates. *J. A. M. A.* 155: 1316-1328, Aug. 7, 1954.
- (6) Doll, R., and Hill, A. B.: The mortality of doctors in relation to their smoking habits. *Brit. Med. J.* No. 4877: 1451-1455, June 26, 1954.
- (7) Morris, J. N., Heady, J. A., Raffle, P. A. B., Roberts, C. G., and Parks, J. W.: Coronary heart disease and physical activity of work. *Lancet* 2: 1053-1057; 1111-1120, Nov. 21, 28, 1953.
- (8) Smillie, W. G., and Hahn, R. G.: Inherent inadequacies of multiphasic screening. *New York State J. Med.* 52: 2610-2611, Nov. 1, 1952.
- (9) Levin, M. L., and Brightman, J.: The place of multiphasic screening in the chronic disease program. *New York State J. Med.* 52: 2600-2604, Nov. 1, 1952.
- (10) Guiss, L.: Mass roentgenographic screening as a lung cancer control measure. *Cancer* 8: 219-236, March-April, 1955.
- (11) Dunn, J. E., and Sprunt, D. H.: Uterine cancer case finding by vaginal cytology. Memphis and Shelby County, Tennessee. *Pub. Health Rep.* 70: 341-346, April 1955.
- (12) Reed, L. J.: Editorial. *J. Chron. Dis.* 1: 86-87, January 1955.
- (13) Roberts, D. W.: The over-all picture of long-term illness. *J. Chron. Dis.* 1: 149-159, February 1955.

technical publications

Education for the Professions

Office of Education Publication. By Lloyd E. Blanch. 1955. 317 pages. Paper, \$1.75; buckram, \$2.75.

This detailed and extensive sourcebook on education for the leading professions in the United States describes these professions and reports on their development and current status of education. It indicates some of the major problems in professional education, lists schools offering professional curriculums, and presents additional reference information.

Twelve chapters are devoted to the health professions: chiropody, dentistry, hospital administration, medicine, nursing, occupational therapy, optometry, osteopathy, pharmacy, physical therapy, public health, and veterinary medicine. Other fields

include accountancy, agriculture, architecture, business administration, engineering, forestry, home economics, journalism, law, library service, music, public administration, social work, teaching, and theology. There are also chapters covering the education of officers in the Army, Navy, Marine Corps, Air Force, Coast Guard, and Merchant Marine.

Outpatient Psychiatric Clinics, 1954

Public Health Service Publication No. 428. 1955. 44 pages. 35 cents.

The first in a series of publications compiled in connection with the new national mental health clinic statistics program, this listing is intended to serve as an interim reference on existing clinics. It is for

the use of professional personnel in community agencies throughout the country.

Name and address of each facility meeting a uniform definition of an outpatient psychiatric clinic are listed by State and location. Appendix A gives headquarters of clinic outlets by State and appendix B, agencies designated as State and Territorial mental health authorities.

This section carries announcements of all new Public Health Service publications and of selected new publications on health topics prepared by other Federal Government agencies.

Publications for which prices are quoted are for sale by the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C. Orders should be accompanied by cash, check, or money order and should fully identify the publication. Public Health Service publications which do not carry price quotations, as well as single sample copies of those for which prices are shown, can be obtained without charge from the Public Inquiries Branch, Public Health Service, Washington 25, D. C.

The Public Health Service does not supply publications issued by other agencies.